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09/600,659	07/20/2000	Tommy Abrahamsson	1103326 0629	9094

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White & Case  
Patent Department  
1155 Avenue of the Americas  
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EXAMINER

LUKTON, DAVID

ART UNIT

PAPER NUMBER

1653

DATE MAILED: 06/10/2003

4

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/600,659

Applicant(s)

ABRAHAMSSON ET AL.

Examiner

David Lukton

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 30 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 2-23,25-33 and 41-63 is/are pending in the application.
- 4a) Of the above claim(s) 3,9-23,25-33 and 43-63 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2,4-8,41 and 42 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

Pursuant to the directives of paper No. 9 (filed 5/3/02), claim 1 has have been cancelled, and claims 2-8, 18, 28, 33, 41, 42 amended. Claims 2-23, 25-33, 41-63 remain pending.

Applicants' arguments filed 5/3/02 have been considered and found persuasive.

Claims 2, 4-8, 41, 42 are examined in this Office action.

Applicants have requested rejoinder of the "kit" claims. In response, it is suggested that the limitations on the CPU inhibitor that is present in claim 2 be introduced into the "kit" claims.

As indicated previously, the abbreviation "CPU" hereinbelow refers to carboxypeptidase U.

\*

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each

claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 2, 4-8, 41, 42 are rejected under 35 U.S.C. §103 as being unpatentable over Ondetti (*Biochem* 18, 1427, 1979) in view of Bajzar (USP 5,993,815) further in view of Bylund (USP 5,955,433) or Antonsson (WO 94/29336) or Lofroth (WO 96/16671).

Ondetti discloses that the compound designated SQ 24,798 is an inhibitor of CPU. As it happens, this compound falls within the scope of instant claim 2 when the variables correspond as follows:

R1-X = guanidinopropyl  
Y = -CH<sub>2</sub>-  
R2 = hydrogen  
R3 = -COOH  
R4 = -SH

Ondetti does not suggest combining a CPU inhibitor with a thrombin inhibitor.

As indicated previously, Bajzar discloses that inhibitors of carboxypeptidase U can be used to to treat thrombosis, stroke, and myocardial infarction. Bajzar does not teach that thrombosis, stroke, or myocardial infarction should be treated with a thrombin inhibitor. Bylund and Antonsson both teach treatment of cardiovascular disorders (Bylund: col 6, line 37+; Antonsson: pages 43-45).

Thus, given that the Ondetti compounds can be used to treat cardiovascular disorders, and that the same is true of thrombin inhibitors, a cardiologist of ordinary skill would have been motivated to combine a CPU inhibitor with a thrombin inhibitor for additive effects.

Thus, the claims are rendered obvious.

※

Claims 2, 4, 5, 8, 41, 42 are rejected under 35 U.S.C. §103 as being unpatentable over Ondetti (USP 4,177,277) in view of Bajzar (*J Biol Chem* **271** 16603, 1996) or Boffa (*J Biol Chem* **273** 2127, 1998).

As indicated previously, Ondetti discloses (col 3, line 18+) compounds that are inhibitors of carboxypeptidase U and as such are useful in the treatment of inflammatory or cardiovascular disorders. For example, the following compound is encompassed by instant claim 2 as well as the prior art genus (applicants' variables are used hereinbelow):

R1-X = aminopropyl  
Y = -CH<sub>2</sub>-  
R2 = hydrogen  
R3 = -COOH  
R4 = -SH

Ondetti does not suggest combining these compounds with thrombin inhibitors. Bajzar and Boffa both teach that CPU is formed by the action of thrombin. Neither Bajzar nor Boffa suggests combining a CPU inhibitor with a thrombin inhibitor. However, given that thrombin is instrumental in the formation of CPU, one of ordinary skill would have been motivated to combine a thrombin inhibitor with a CPU inhibitor to achieve additive effects, i.e., inhibition of the formation of CPU, and inhibition of whatever CPU happens to be formed.

Thus, the claim is rendered obvious.

✱

Claims 2, 4, 5, 8, 41, 42 are rejected under 35 U.S.C. §103 as being unpatentable over Ondetti (USP 4,177,277) in view of Grainger (USP 6,410,587) or Watson (USP 6,326,386) or Franson (USP 6,020,510).

Ondetti discloses (col 3, line 18+) compounds that are inhibitors of carboxypeptidase U and as such are useful in the treatment of inflammation. These compounds fall within the scope of instant claim 2. Ondetti does not suggest combining these compounds with thrombin inhibitors. Each of the secondary references teaches that thrombin inhibitors can be used to treat inflammation, or else that compounds exist which are useful to treat inflammation, and at the same time inhibit thromin. Relevant passages are as follows:

- Grainger discloses (col 22, line 32+) compounds which serve the dual role of thrombin inhibitor and anti-inflammatory agent.
- Franson discloses (col 7, line 58+) compounds that inhibit thrombin-induced platelet aggregation, and at the same time, can be used to treat various inflammatory conditions.
- Watson discloses (col 1, lin 55+) that thrombin inhibitors can be used to treat inflammation

Thus, one of ordinary skill would have been motivated to combine the anti-inflammatory compounds of Ondetti with the anti-inflammatory compounds of the secondary references. The resulting compositions would then contain an inhibitor of CPU as well as an inhibitor

of thrombin.

Thus, the claim is rendered obvious.

※

Claims 2, 4, 5, 8, 41, 42 are rejected under 35 U.S.C. §103 as being unpatentable over Eisenbach-Schwartz (USP 6,126,939) in view of Grainger (USP 6,410,587) or Watson (USP 6,326,386) or Franson (USP 6,020,510).

Eisenbach-Schwartz discloses (col 3, line 37) that the dipeptide Arg-Cys can be used to treat various inflammatory disorders, such as those recited in cols 5-6 of the reference.

This compound is encompassed by formula I of claim 2 when the substituent variables correspond as follows:

R1-X	=	C <sub>4</sub> -alkyl substituted with two basic groups
Y	=	-CH <sub>2</sub> -
R2	=	hydrogen
R3	=	-COOH
R4	=	-SH

The reference does not disclose that this dipeptide is an inhibitor of CPU, but this property is inherent, absent evidence to the contrary. Eisenbach-Schwartz does not suggest combining this dipeptide with a thrombin inhibitor. As indicated previously, each of the secondary references teaches that thrombin inhibitors can be used to treat inflammation, or else that compounds exist which are useful to treat inflammation, and at the same time inhibit thrombin.

\*

Claims 2, 4-8, 41, 42 are rejected under 35 U.S.C. §103 as being unpatentable over Eisenbach-Schwartz (USP 6,126,939) in view of Antonsson (WO 94/29336).

As indicated above, Eisenbach-Schwartz discloses (col 3, line 37) that the dipeptide Arg-Cys can be used to treat various inflammatory disorders, such as those recited in cols 5-6 of the reference. For example, treatment of arthritis is disclosed at col 5, line 15.

Eisenbach-Schwartz does not suggest combining this dipeptide with a thrombin inhibitor.

Antonsson discloses various thrombin inhibitors, and asserts (e.g., page 45) that these compounds can be used to treat various inflammatory disorders. For example, treatment of arthritis is disclosed at page 45, line 12.

Thus, an allergist of ordinary skill would have been motivated to combine the dipeptide Arg-Cys with a thrombin inhibitor of Antonsson in order to achieve additive effects in the treatment of inflammatory disorders.

\*

Claims 2, 4-8, 41, 42 are rejected under 35 U.S.C. §103 as being unpatentable over Ondetti (USP 4,177,277) in view of Bylund (USP 5,955,433) or Lofroth (WO 96/16671) or Antonsson (WO 94/29336).

The teachings of the references are given above and/or previously. Ondetti does not suggest combining the CPU inhibitors with a thrombin inhibitor. However, Bylund and



Antonsson both teach that thrombin inhibitors can be used to treat cardiovascular disorders.

In addition, Antonsson discloses that thrombin inhibitors can be used to treat various inflammatory disorders.

Accordingly, the cardiologist of ordinary skill would have been motivated to combine the CPU inhibitors of Ondetti with the thrombin inhibitors of Bylund or Lofroth or Antonsson for additive effects. In addition, the allergist of ordinary skill would have been motivated to combine the CPU inhibitors of Ondetti with the thrombin inhibitors of Antonsson for additive effects.

\*

No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



DAVID LUKTON  
PATENT EXAMINER  
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